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Comparative Analysis of Length of Stay, Total Costs, and Treatment Success between Intravenous Moxifloxacin 400 mg and Levofloxacin 750 mg among Hospitalized Patients with Community-Acquired Pneumonia

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ABSTRACT

Objective: This study aimed to evaluate the length of stay (LOS), costs, and treatment consistency among patients hospitalized with community-acquired pneumonia (CAP) initially treated with intravenous (IV) moxifloxacin 400 mg or IV levofloxacin 750 mg.

Methods: Adults with CAP receiving IV moxifloxacin or IV levofloxacin for ≥3 days were identified in the Premier Perspective comparative database. Primary outcomes were LOS and costs. Secondary outcomes included treatment consistency, which was defined as 1) no additional IV moxifloxacin or levofloxacin after ≥1 day off study drug; 2) no switch to another IV antibiotic; and 3) no addition of another IV antibiotic.

Results: A total of 7720 patients met inclusion criteria (6040 receiving moxifloxacin; 1680 receiving levofloxacin). Propensity matching created two cohorts (1300 patients each) well matched for demographic, clinical, hospital, and payor characteristics. Before the patients were matched, mean LOS (5.87 vs. 5.46 days; $P = 0.0004$) and total costs per patient ($7302 vs. $6362; $P < 0.0001$) were significantly greater with moxifloxacin. After the patients were matched, mean LOS (5.63 vs. 5.51 days; $P = 0.462$) and total costs ($6624 vs. $6473; $P = 0.476$) were comparable in both cohorts. Treatment consistency was higher for moxifloxacin before (81.0% vs. 78.9%; $P = 0.048$) and after matching (82.8% vs. 78.0%; $P = 0.002$).

Conclusions: In-hospital treatment of CAP with IV moxifloxacin 400 mg or IV levofloxacin 750 mg was associated with similar hospital LOS and costs in propensity-matched cohorts.

Keywords: community-acquired pneumonia, cost, hospital, length of stay, levofloxacin, moxifloxacin, treatment outcomes.

Introduction

Community-acquired pneumonia (CAP) occurs in an estimated 5 to 6 million persons annually in the United States and results in approximately 60,000 deaths [1,2]. Each year, CAP is responsible for an estimated 10 million physician visits and more than 1 million hospitalizations [3,4]. A cost-of-illness study found that the total direct cost for treating CAP was $8.4 billion (in 1995 dollars), of which $4.8 billion was for patients ≥65 years of age [1]. Eighty-nine percent of the total cost, or $7.5 billion, was for inpatient care. According to the 2005 Nationwide Inpatient Sample, the average hospital length of stay (LOS) for CAP was 5.52 days, and in-hospital mortality was 4% [5].

The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) recently issued consensus guidelines for the management of adults with CAP to identify patients who should be hospitalized, as well as antibiotics for empiric use before a causative pathogen has been isolated [6]. Several studies have shown that the implementation of the IDSA/ATS guidelines leads to improved patient care with concomitant reductions in hospital LOS, costs, and readmissions [7–9]. Other studies have demonstrated that such reductions in LOS produce substantial cost savings without adversely affecting mortality, readmission rates, or the time needed to return to normal activities [10,11].

The decision to hospitalize a patient is based on the severity of illness and the clinicians' determination of a range of factors, including the likelihood that the patient will reliably take oral medications [6]. The IDSA/ATS guidelines recommend hospitalization or, where available and appropriate, intensive, in-home health-care services, for patients with confusion, urea, respiratory rate, blood pressure, and age ≥65 years scores ≥2. Empiric antibiotic therapy in hospitalized patients should consist of a respiratory fluoroquinolone (e.g., moxifloxacin or levofloxacin) or alternatively, a beta-lactam (e.g., cefotaxime, ceftriaxone, ampicillin, or for selected patients, ertapenem) plus macrolide regimen [6]. When patients are admitted directly to an intensive care unit (ICU), empiric therapy should consist of a beta-lactam plus either a respiratory fluoroquinolone or azithromycin.

The safety and efficacy of respiratory fluoroquinolones in hospitalized patients with CAP have been demonstrated in numerous studies [12–15]. Comparisons to beta-lactam–macrolide regimens or nonstandardized regimens suggest that fluoroquinolones lead to earlier hospital discharge, which in some studies has led to cost savings [16–18]. In the Community-Acquired Pneumonia Recovery in the Elderly study, a prospective, randomized, double-blind trial, treatment with moxifloxacin 400 mg daily was associated with significantly faster clinical recovery than treatment with levofloxacin 500 mg daily in hospitalized elderly patients with CAP, although the clinical cure rates did not differ significantly when assessed 5 to 21 days after completion of treatment [15]. Nevertheless, a recent retrospective database analysis of hospitalized patients with CAP suggested that initial treatment with intravenous (IV) levofloxacin 750 mg reduced hospital LOS by 0.5 day when compared with initial treatment with IV moxifloxacin 400 mg [19]. Comparisons between levofloxacin and moxifloxacin in that study may have been limited by methodological issues. To

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address these issues, we also conducted a retrospective database analysis to evaluate LOS and costs, as well as treatment consistency, among patients with CAP treated with IV moxifloxacin 400 mg or IV levofloxacin 750 mg daily. Our objective was to compare treatment costs and outcomes (LOS and treatment consistency) with moxifloxacin and levofloxacin from the payor's perspective, in propensity-matched cohorts of hospitalized patients with CAP.

Methods

Data Source

Data from the Premier Perspective comparative database (PCD; Charlotte, NC) from April 2003 to March 2006 were analyzed. The PCD contains inpatient data from more than 500 acute-care facilities in the United States that represent all geographic areas, urban and rural facilities, teaching and nonteaching hospitals, and a broad range of hospital sizes [20]. The database includes standard hospital admission and discharge information as well as date-stamped logs of all billed items for procedures, medications, and laboratory, diagnostic, and therapeutic services at the individual patient level. Hospitals submit data to the PCD on a monthly or quarterly basis. The data undergo extensive quality assurance and data validation checks, and the cost information is reconciled with the hospitals' financial statements before the data are made available for research.

Eligibility Criteria

Patients ≥18 years of age with a principal diagnosis of *CAP* [*International Classification of Diseases, Ninth Revision* (*ICD-9*) codes: 481, 482.xx, 483.xx, 485, 486, and 487.x] who were treated for ≥3 days with either IV moxifloxacin 400 mg or IV levofloxacin 750 mg beginning on the date of hospital admission or on the following day were identified [21,22]. Patients who were admitted from or discharged to another acute-care hospital, nursing home, or other long-term care facility and those discharged from the hospital in the previous month were excluded to ensure that the pneumonia episode was community acquired and not nosocomial and that only complete episodes of inpatient care were examined. Patients were also excluded if they were discharged with surgical diagnosis-related groups (DRGs) (i.e., only patients with DRGs 79, 80, 89, 90, 475, and 565 were eligible), received a first IV dose with an antibiotic other than moxifloxacin or levofloxacin, switched antibiotic therapy during the first 3 days of hospitalization, had a hospital LOS of <3 days, or had a discharge status of death.

Patient Population

The patient population was characterized by a series of demographic and clinical variables, payor and provider variables, and medication-related variables. The demographic variables included patient age, sex, race, and year of admission. Clinical variables included the type of pneumonia based on the three-digit level principal discharge *ICD-9* code, and comorbidities and CAP complications derived from the secondary diagnosis *ICD-9* codes in the admission record. The CAP complications provide a measure of initial CAP severity and include sepsis, respiratory failure, pleural effusion and empyema, abscess, renal failure, and congestive heart failure. In addition, the severity of illness and risk of mortality were assessed by using the All Patient Refined DRG (APR-DRG). Other severity-related clinical variables that were captured included intubation at any time during an admission, respiratory therapy within the first 24 hours after admission, and total length of stay in the ICU. Payor data were grouped into the following categories: Medicare, Medicaid, private insurance, uninsured, other, and unknown. Provider data were characterized by region (Northeast, Midwest, South, and West), location (urban or rural), teaching hospital status, number of beds, admission from the emergency department, and specialty of the admitting and attending physicians. Medication-related variables included the number of doses of study drug that were administered during the hospital stay and the average daily dose of the study drug.

Outcome Variables

The primary outcome variables were total costs (in US dollars) per hospital admission with CAP and LOS per admission with CAP. The LOS represented the total number of days in the hospital, from the day of admission to the day of discharge. Because this study covered a 3-year period, total costs for the index hospitalization were calculated according to the discharge month and then standardized into March 2006 dollars by using the corresponding Consumer Price Index Medical Care for that month. The costs for the components of care—a secondary outcome variable—were identified by using UB-92 revenue codes and standardized by using the Consumer Price Index Medical Care. These costs included room and board (UB-92 revenue codes 110–219), pharmacy (codes 25x and 63x), IV therapy supplies (code 26x), respiratory therapy (code 41x), and all other costs (identified by other revenue codes). Other secondary outcome variables included treatment consistency. Treatment consistency was achieved if the patients met all of the following three criteria: 1) they did not require an additional dose of IV moxifloxacin or levofloxacin during the same hospital stay after being off the study drug for at least 1 day (retreatment); 2) they did not switch to another IV antibiotic (switch); and 3) they did not require the addition of another IV antibiotic (add-on).

Statistical Analyses

Statistical analysis was performed by using Statistical Analysis Software (SAS; SAS Institute Inc., Cary, NC). The conditional logistic regression analysis was conducted by using SAS 9.1, and the rest of the analyses were conducted by using SAS 8.2. Baseline demographic and other information were presented because either counts (%) for categorical data or mean (SD) for continuous data. Descriptive profiles were calculated for all variables before and after propensity score matching. Categorical variables were evaluated by using chi-square tests, and continuous variables were analyzed by using nonparametric rank-sum tests.

Outcomes were compared in three different manners: prematched unadjusted comparison, postmatched unadjusted comparison, and postmatched comparison adjusted for factors thought to influence outcome. Because patients were not randomly allocated to study treatment, propensity score matching was used to develop comparable cohorts of patients treated with IV moxifloxacin and IV levofloxacin having similar distributions of patient characteristics [23]. The probability that a patient received moxifloxacin as the index drug was modeled by using demographics, hospital characteristics, and baseline clinical characteristics. Variables that affect treatment choice and outcomes were included in the matching process, including age, sex, race, type of pneumonia, severity measures, comorbidities, CAP complications, type of payor, hospital teaching status, hospital size, region, location, admitting and attending physician specialty, emergency department admission, and year of admission. The logistic regression model was constructed in a stepwise manner to predict the probability of moxifloxacin use by each patient.

Table 1 Demographic and clinical characteristics of the moxifloxacin and levofloxacin cohorts before and after matching

Characteristic	Before matching			After matching		
	Moxifloxacin (N = 6040)	Levofloxacin (N = 1680)	*P*-value	Moxifloxacin (N = 1300)	Levofloxacin (N = 1300)	*P*-value
Sex, no. (%)						
Male	2442 (40.4)	686 (40.8)	0.766	553 (42.5)	536 (41.2)	0.499
Female	3598 (59.6)	994 (59.2)		747 (57.5)	764 (58.8)	
Age, mean (SD), year	70.5 (15.2)	68.4 (15.7)	<0.0001	69.2 (15.2)	69.1 (15.6)	0.986
Comorbid conditions, no. (%)						
Cancer	417 (6.9)	127 (7.6)	0.353	100 (7.7)	92 (7.1)	0.549
Diabetes	1941 (32.1)	510 (30.4)	0.166	399 (30.7)	403 (31.0)	0.865
COPD	3239 (53.6)	1061 (63.2)	<0.0001	812 (62.5)	814 (62.6)	0.935
Asthma	3769 (62.4)	1320 (78.6)	<0.0001	991 (76.2)	989 (76.1)	0.927
Cardiovascular disease	1898 (31.4)	431 (25.7)	<0.0001	353 (27.2)	351 (27.0)	0.930
Secondary diagnoses, mean (SD), no.	7.63 (3.76)	7.38 (3.57)	0.072	7.72 (3.96)	7.44 (3.44)	0.369
Any CAP complication, no. (%)	5187 (85.9)	1406 (83.7)	0.025	1105 (85.0)	1099 (84.5)	0.743
Sepsis	177 (2.9)	96 (5.7)	<0.0001	59 (4.5)	62 (4.8)	0.780
Respiratory failure	3903 (64.6)	1088 (64.8)	0.914	874 (67.2)	852 (65.5)	0.361
Pleural effusion/empyema	319 (5.3)	95 (5.7)	0.548	65 (5.0)	79 (6.1)	0.230
Abscess	16 (0.3)	8 (0.5)	0.169	4 (0.3)	5 (0.4)	0.738
Renal failure	1548 (25.6)	427 (25.4)	0.860	361 (27.8)	364 (28.0)	0.896
Congestive heart failure	2758 (45.7)	678 (40.4)	0.0001	535 (41.2)	532 (40.9)	0.905
APR-DRG severity, no. (%)						
Minor	485 (8.0)	171 (10.2)	<0.0001	106 (8.2)	124 (9.5)	0.270
Moderate	3154 (52.2)	934 (55.6)		701 (53.9)	726 (55.8)	
Major	2170 (35.9)	532 (31.7)		454 (34.9)	417 (32.1)	
Extreme	231 (3.8)	43 (2.6)		39 (3.0)	33 (2.5)	
APR-DRG mortality risk, no. (%)						
Minor	1784 (29.5)	620 (36.9)	<0.0001	452 (34.8)	455 (35.0)	0.977
Moderate	3312 (54.8)	854 (50.8)		678 (52.2)	678 (52.2)	
Major	822 (13.6)	179 (10.7)		153 (11.8)	148 (11.4)	
Extreme	122 (2.0)	27 (1.6)		17 (1.3)	19 (1.5)	
Patients intubated, no. (%)	59 (1.0)	8 (0.5)	0.050	6 (0.5)	8 (0.6)	0.592
Patients receiving respiratory therapy, no. (%)	5130 (84.9)	1528 (91.0)	<0.0001	1166 (89.7)	1168 (89.8)	0.897

APR-DRG,All Patient Refined Diagnostic-Related Groups; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disorder. *P*-values are the result of bivariate comparisons.

After the logistic regression model was estimated, individuals in the moxifloxacin cohort were matched one to one with the pool of levofloxacin users who had similar propensity scores using a greedy match [24]. Sampling without replacement was used when creating the propensity-matched samples. The quality of the match was examined by using descriptive statistics tests, including chi-square and rank-sum tests. A multivariate analysis was performed on the matched samples to examine the marginal effects of specific factors on outcomes of interest. Generalized linear models were used when costs and cost components were the outcome (Gamma distribution), count data models (Poisson regression) were used for LOS, and a conditional logistic model stratified on the match was used for treatment consistency. Independent variables included in these models were demographic and clinical characteristics, payor, hospital characteristics, physician specialty, emergency department admission, year of admission, and treatment with moxifloxacin or levofloxacin. For the multivariate analysis related to LOS and the GLM related to total costs, *P*-values and Wald 95% confidence intervals (CI) are presented from the models without any adjustments.

Results

Patient Cohorts

A total of 34,287 patients with CAP who were discharged after receiving either moxifloxacin or levofloxacin during the 3-year study period were identified in the PCD. Of these, 6040 (25.4%) of 23,746 patients who received moxifloxacin and 1680 (15.9%) of 10,541 patients who received levofloxacin met eligibility criteria and were included in this analysis.

The unmatched moxifloxacin and levofloxacin cohorts differed significantly in terms of a variety of demographic, clinical, and hospital characteristics. Patients who received moxifloxacin tended to be older [mean (SD) age, 70.5 (15.2) vs. 68.4 (15.7) years; $P < 0.0001$], were more likely to have comorbid cardiovascular disease, and were less likely to have chronic obstructive pulmonary disorder or asthma (all $P < 0.0001$) (Table 1). The severity of illness estimated by APR-DRG severity and risk of mortality were generally higher in the moxifloxacin group (both $P < 0.0001$), whereas CAP complications were generally evenly balanced between groups, apart from congestive heart failure, which was more common in the moxifloxacin group (45.7% vs. 40.4%; $P = 0.0001$), and sepsis, which was more common in the levofloxacin group (2.9% vs. 5.7%; $P < 0.0001$). In terms of hospital characteristics, patients in the moxifloxacin group were more likely to be treated at a teaching hospital (49.1% vs. 38.5%; $P < 0.0001$), in an urban location (93.4% vs. 77.9%; $P < 0.0001$), and/or at a larger facility [mean (SD) number of beds = 465 (226) vs. 379 (214); $P < 0.0001$], and to be admitted from the emergency department (84.7% vs. 76.3%; $P < 0.0001$) (Table 2). The distribution by hospital region, year of admission, and admitting physician specialty also differed significantly between groups (all $P < 0.0001$).

Propensity matching produced a total sample of 2600 patients, equally divided between the moxifloxacin and levofloxacin cohorts. After matching, there were no statistically significant differences between the two cohorts in terms of demographic, clinical, hospital, or payor characteristics (Tables 1 and 2). For the two combined cohorts, the mean age was 69 years; the majority were female (58%) and/or had comorbid asthma (76%) or chronic obstructive pulmonary disorder (63%). Most patients had at least one CAP complication (85%), most commonly respiratory failure (66%), and slightly more than half (55%) had moderate APR-DRG severity. Less than 1% of

Table 2 Payor and hospital characteristics of the moxifloxacin and levofloxacin cohorts before and after matching

Characteristic	Before matching			After matching		
	Moxifloxacin (N = 6040)	Levofloxacin (N = 1680)	*P*-value	Moxifloxacin (N = 1300)	Levofloxacin (N = 1300)	*P*-value
Payor type, no. (%)						
Medicare	4152 (68.7)	1122 (66.8)	<0.0001	894 (68.8)	896 (68.9)	0.979
Medicaid	299 (5.0)	114 (6.8)		76 (5.8)	81 (6.2)	
Private insurance	1296 (21.5)	295 (17.6)		241 (18.5)	233 (17.9)	
Uninsured	184 (3.0)	81 (4.8)		48 (3.7)	51 (3.9)	
Other	109 (1.8)	68 (4.0)		41 (3.2)	39 (3.0)	
Hospital region, no. (%)						
Northeast	1572 (26.0)	196 (11.7)	<0.0001	188 (14.5)	196 (15.1)	0.585
Midwest	1301 (21.5)	415 (24.7)		332 (25.5)	343 (26.4)	
South	2817 (46.6)	868 (51.7)		655 (50.4)	622 (47.8)	
West	350 (5.8)	201 (12.0)		125 (9.6)	139 (10.7)	
Population density, no. (%)						
Rural	399 (6.6)	371 (22.1)	<0.0001	200 (15.4)	187 (14.4)	0.474
Urban	5641 (93.4)	1309 (77.9)		1100 (84.6)	1113 (85.6)	
Teaching hospital, no. (%)	2963 (49.1)	646 (38.5)	<0.0001	561 (43.2)	574 (44.2)	0.607
Hospital size, mean (SD) beds, no.	465.1 (226.4)	378.6 (213.9)	<0.0001	389.0 (69.2)	390.5 (208.9)	0.637
Year of admission, no. (%)						
2003	1119 (18.5)	16 (1.0)	<0.0001	19 (1.5)	16 (1.2)	0.559
2004	1988 (32.9)	201 (12.0)		217 (16.7)	193 (14.8)	
2005	2267 (37.5)	861 (51.3)		681 (52.4)	704 (54.2)	
2006	666 (11.0)	602 (35.8)		383 (29.5)	387 (29.8)	
Admission from emergency department, no. (%)	5117 (84.7)	1282 (76.3)	<0.0001	1036 (79.7)	1024 (78.8)	0.562
Admitting physician specialty, no. (%)						
Hospitalist	29 (0.5)	122 (7.3)	<0.0001	29 (2.2)	14 (1.1)	0.207
Infectious disease	10 (0.2)	1 (0.1)		2 (0.2)	1 (0.1)	
Primary care	4360 (72.2)	1238 (73.7)		1012 (77.8)	1015 (78.1)	
Pulmonologist	299 (5.0)	114 (6.8)		89 (6.8)	93 (7.2)	
Other	1342 (22.2)	205 (12.2)		168 (12.9)	177 (13.6)	

P-values are the result of bivariate comparisons.

patients were intubated. Most patients were treated at an urban hospital (85%), had Medicare coverage (69%), were admitted in the year 2005 (52%), and/or were admitted after presentation to the emergency department (79%).

Outcomes

Before propensity matching, the mean (SD) LOS was significantly longer (0.41 day) in the moxifloxacin than in the levofloxacin cohort [5.87 (4.10) vs. 5.46 (3.45) days, respectively; $P = 0.0004$] (Fig. 1). Nevertheless, after propensity score matching, there was no significant difference in LOS between the moxifloxacin and levofloxacin groups [5.63 (3.50) vs. 5.51 (3.52) days; $P = 0.462$]. Total hospital costs showed a similar profile, with moxifloxacin versus levofloxacin having higher average total costs in the unmatched population [$7302 ($10,754) vs. $6362 ($4654), respectively; $P < 0.0001$], but no significant differences in the propensity-matched cohorts [$6624 ($5576) vs. $6473 ± ($4782); $P = 0.476$] (Fig. 2).

Similarly, when individual cost components were evaluated, higher room and board charges ($P < 0.0001$) and pharmacy costs ($P = 0.0003$) were found in the moxifloxacin group than in the levofloxacin group before matching. After propensity matching, room and board charges ($P = 0.239$) and pharmacy costs ($P = 0.905$) did not differ significantly between the moxifloxacin and levofloxacin cohorts (Table 3). The numeric difference between the two matched cohorts was $103 for room and board costs and $33 for pharmacy costs. The cost of IV

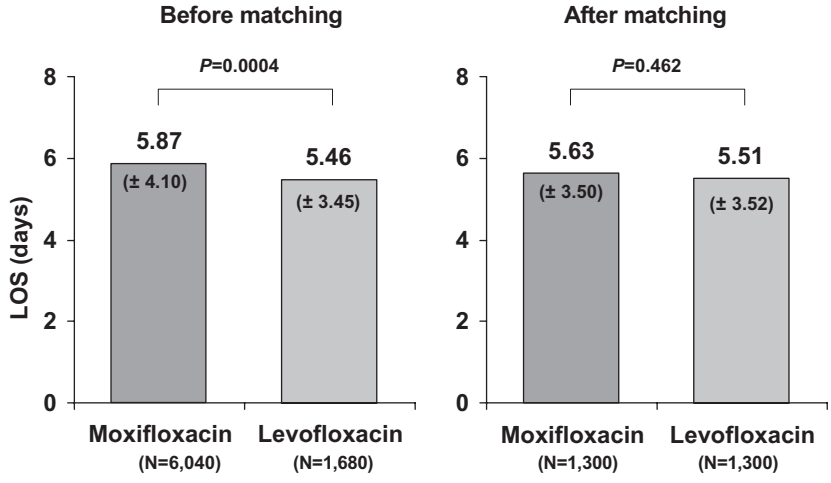

Figure 1 Mean length of stay (standard deviation) in moxifloxacin and levofloxacin cohorts before and after matching. *P*-values are the result of bivariate comparisons.

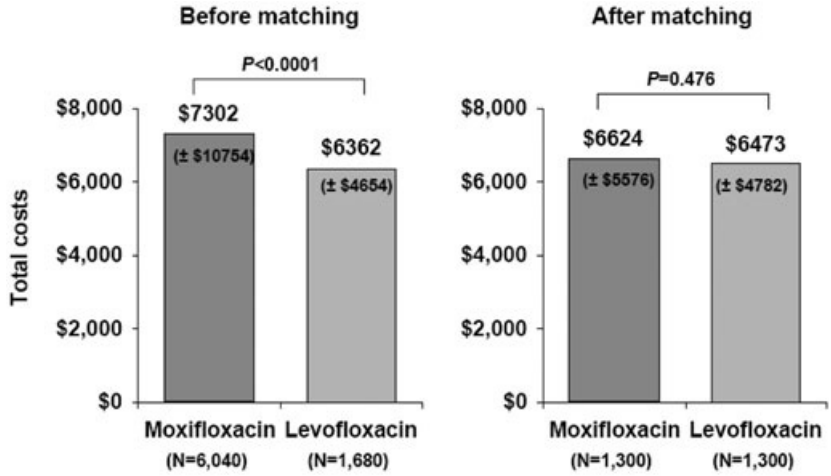

Figure 2 Total costs (standard deviation) in moxifloxacin and levofloxacin cohorts before and after matching. *P*-values are the result of bivariate comparisons.

therapy supplies was higher in the levofloxacin group than in the moxifloxacin group both before ($P < 0.0001$) and after ($P = 0.0006$) propensity matching; the differences between treatment cohorts were $10 and $25, respectively. Respiratory therapy costs and other costs did not differ between groups in the prematched cohorts, whereas after matching, respiratory therapy costs were $112 higher in the moxifloxacin group ($P < 0.0001$), and other costs were $71 higher in the levofloxacin group ($P = 0.0043$).

Moxifloxacin was associated with a significantly higher treatment consistency than levofloxacin before propensity matching (81.0% vs. 78.9%, respectively; $P = 0.0481$) as well as after matching (82.8% vs. 78.0%; $P = 0.0018$) (Fig. 3). These findings reflected differences in retreatment rates (defined as requiring an additional dose of IV moxifloxacin or levofloxacin during the same hospital stay after being off the study drug for at least 1 day), which were higher in the levofloxacin group before propensity matching (13.6% vs. 11.9%, respectively; $P = 0.060$) and significantly higher in the levofloxacin group after matching (14.1% vs. 9.2%; $P < 0.0001$). Frequencies of regimen changes from one study drug to another or to add-on therapy did not differ between the moxifloxacin and levofloxacin cohorts before or after propensity matching.

Factors Influencing Outcomes

Tables 4 and 5 present factors that significantly affected LOS (Table 4) and total costs (Table 5). In the multivariate analysis, the choice of index drug (moxifloxacin vs. levofloxacin) was not significant in the estimation of the LOS (Table 4; 95% CI for index drug regression coefficient = –0.027 to 0.039) or the total costs (Table 5; 9% CI for index drug regression coefficient = –0.048 to 0.025). On the other hand, a number of other demographic, clinical, and hospital factors were significant predictors of one or both of these outcomes, resulting in models with some predictive power; adjusted $R^2 = 0.33$ and adjusted $R^2 = 0.24$ for the multivariate model for total costs and LOS, respectively.

Clinical factors that were significantly associated with LOS included the need for intubation, the presence of an abscess, an *ICD-9* code for other bacterial pneumonia, the presence of pleural effusion or empyema, the presence of congestive heart failure, and the number of secondary diagnoses at admission (all $P < 0.0001$) as well as APR-DRG severity ($P = 0.0001$). Female sex ($P < 0.0001$) and advanced age ($P = 0.001$) were the only demographic factors that emerged as significant predictors of LOS, whereas Medicare insurance ($P = 0.0029$) and other forms of insurance (i.e., not Medicare, Medicaid, or private insurance) ($P = 0.0009$) were significantly associated with shorter mean LOS. Hospital factors significantly associated with longer LOS included nonteaching facility, Northeast region, and admission in 2004 or 2005.

In general, the foregoing factors were also significantly associated with total hospital costs (Table 5). The proportion of the LOS spent in the ICU strongly influenced total costs ($P < 0.0001$), as did the need for intubation ($P < 0.0001$). Several hospital characteristics, including nonteaching status, Northeast region, rural location, admission in 2004, and admission from

Table 3 Medical costs and length of stay of moxifloxacin and levofloxacin cohorts before and after matching

	Before matching			After matching		
Outcome	Moxifloxacin (N = 6040)	Levofloxacin (N = 1680)	*P*-value	Moxifloxacin (N = 1300)	Levofloxacin (N = 1300)	*P*-value
Mean (SD) cost per patient, US$						
Total cost	7,302 (10,754)	6,362 (4,654)	<0.0001	6,624 (5,576)	6,473 (4,782)	0.476
Room and board	4,108 (8,709)	3,326 (2,753)	<0.0001	3,536 (3,081)	3,433 (2,849)	0.239
Pharmacy	624 (951)	589 (743)	0.0003	620 (817)	587 (791)	0.905
IV therapy supplies	194 (251)	204 (265)	<0.0001	177 (211)	202 (284)	0.0006
Respiratory therapy	467 (792)	387 (646)	0.992	496 (853)	384 (700)	<0.0001
Other	1,099 (3,922)	1,855 (1,596)	0.293	1,796 (1,808)	1,867 (1,610)	0.0043
Mean (SD) length of stay, d	5.87 (4.10)	5.46 (3.45)	0.0004	5.63 (3.50)	5.51 (3.52)	0.462

IV, intravenous. *P*-values are the result of bivariate comparisons.

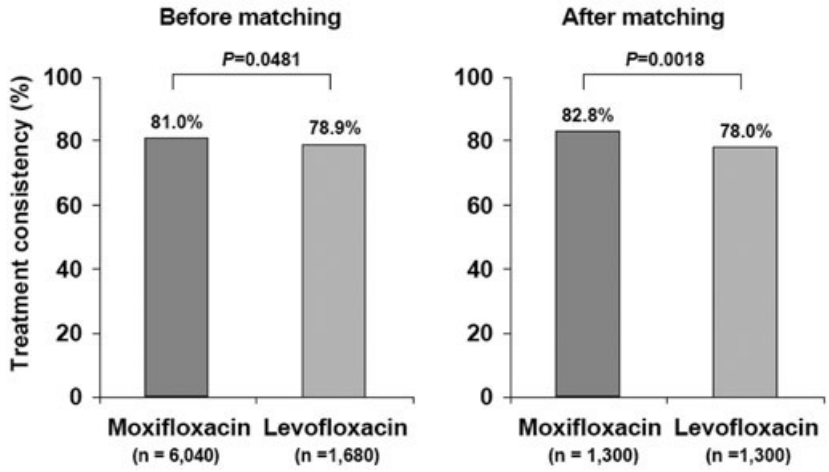

Figure 3 Treatment consistency in moxifloxacin and levofloxacin cohorts before and after matching. *P*-values are the result of bivariate comparisons.

the emergency department, were significantly predictive of total costs (Table 5), but payor factors were not (data not shown).

Patients treated with moxifloxacin were more likely to achieve treatment consistency than those receiving levofloxacin [odds ratio (OR) = 1.40; $P = 0.0048$, global null hypothesis likelihood ratio $P < 0.001$]. Regardless of whether patients received moxifloxacin or levofloxacin, they were less likely to achieve treatment consistency if they had a higher number of secondary diagnoses (OR = 0.914; $P = 0.001$) or a higher APR-DRG risk of mortality (OR = 0.638; $P = 0.015$). No other demographic, clinical, hospital, or payor characteristic was a significant predictor of treatment consistency.

Discussion

Results of the present study indicate that neither clinical nor formulary decisions concerning levofloxacin or moxifloxacin for CAP can be made strictly on the basis of different costs of care, including LOS. This retrospective database analysis demonstrated that daily IV treatment with moxifloxacin 400 mg or levofloxacin 750 mg was associated with similar hospital LOS and total costs in a matched cohort of patients with CAP. Before propensity matching, the moxifloxacin and levofloxacin cohorts differed considerably in demographic and clinical characteristics known to influence LOS and costs, such as advanced age, illness severity, and mortality risk, as well as in various hospital- and payor-based characteristics that can also impact these outcomes. Because patients were not randomly allocated to moxifloxacin or levofloxacin treatment, estimation of treatment effects on LOS and costs may be biased by such imbalances between treatment groups. Accordingly, comparisons of outcomes between cohorts receiving one of the two fluoroquinolones before successful propensity matching are not a reliable means of concluding that LOS or total costs differ between moxifloxacin and levofloxacin.

Propensity score matching was developed to reduce bias between two imbalanced study groups. Heckman and colleagues

Table 4 Results of multivariate analysis of variables associated with length of stay (LOS)

Variable	Estimated coefficients	Wald 95% CI	*P*-value
Moxifloxacin	0.0057	–0.027 to 0.039	0.734
Demographic factors			
Age	0.0027	0.001–0.004	0.001
Female	0.0707	0.036–0.105	<0.0001
Clinical factors			
ICD-9 code 482 (other bacterial pneumonia)	0.2588	0.198–0.320	<0.0001
Comorbid cancer	0.1026	0.040–0.166	0.0014
Comorbid cardiovascular disease	–0.0552	–0.016 to –0.094	0.0057
Number of secondary diagnoses	0.0324	0.027–0.038	<0.0001
Respiratory failure	0.0679	0.017–0.118	0.0085
Pleural effusion and empyema	0.2117	0.146–0.278	<0.0001
Abscess	0.5152	0.326–0.705	<0.0001
Congestive heart failure	0.0845	0.045–0.124	<0.0001
APR-DRG severity	0.0721	0.037–0.107	0.0001
Intubation	0.6014	0.432–0.770	<0.0001
Hospital factors			
Nonteaching hospital	0.0583	0.014–0.102	0.0095
Northeast region	0.1537	0.077	<0.0001
Admission in 2004	0.0852	0.032–0.138	0.0016
Admission in 2005	0.0534	0.015–0.092	0.0068
Payor factors			
Medicare	–0.1456	–0.050 to –0.242	0.0029
Other	–0.2277	–0.093 to –0.362	0.0009

Overall model: Adjusted $r^2 = 0.24$; chi-square test for model $P < 0.0001$.
APR-DRG, All Patient Refined Diagnostic-Related Groups; CI, confidence interval; *ICD-9*, *International Classification of Diseases, Ninth Revision.*

Table 5 Results of generalized linear model analysis of variables associated with total costs

Variable	Estimated coefficients	Wald 95% CI	*P*-value
Moxifloxacin	−0.0155	−0.048 to 0.025	0.532
Demographic factors			
Female	0.0611	0.023–0.099	0.0015
Clinical factors			
ICD-9 code 482 (other bacterial pneumonia)	0.233	0.156–0.310	<0.0001
Comorbid cancer	0.1831	0.110–0.257	<0.0001
Comorbid COPD	0.1063	0.059–0.154	<0.0001
Number of secondary diagnoses	0.0349	0.029–0.041	<0.0001
Pleural effusion and empyema	0.1942	0.110–0.278	<0.0001
Abscess	0.5179	0.205–0.831	0.0012
Renal failure	0.0648	0.017–0.113	0.0083
Congestive heart failure	0.1571	0.113–0.201	<0.0001
APR-DRG severity	0.0759	0.037–0.115	0.0001
Intubation	0.5931	0.325–0.861	<0.0001
Respiratory therapy	0.1189	0.049–0.189	0.0008
% of LOS spent in ICU	0.5987	0.396–0.802	<0.0001
Hospital factors			
Nonteaching hospital	0.0657	0.017–0.114	0.0079
Northeast region	0.1246	0.040–0.210	0.0040
Rural location	−0.1063	−0.049 to −0.164	0.0003
Admission in 2004	0.1521	0.094–0.211	<0.0001
Emergency department admission	−0.0909	−0.045 to −0.137	0.0001

Overall model: Adjusted $r^2 = 0.33$; chi-square test for model $P < 0.0001$.
APR-DRG, All Patient Refined Diagnostic-Related Group; CI, confidence interval; COPD, chronic obstructive pulmonary disorder, *ICD-9*, *International Classification of Diseases, Ninth Revision*; ICU, intensive care unit; LOS, length of stay.

suggested that up to 85% of the bias resulting from unequal distributions in patient characteristics can be neutralized by matching patients by using propensity scores [23]. Multiple methods have been developed for conducting propensity matching, including stratified matching, nearest-neighbor matching, radius matching, kernel matching, and Mahalanobis matching [23–26]. When there is considerable overlap in the estimated propensity score between groups, as is the case in the present study, each matching method should provide similar estimated treatment effects [26]. After propensity score matching, the moxifloxacin and levofloxacin cohorts were well balanced, with no significant differences between groups in admission demographic, clinical, hospital, or payor characteristics. This supports the conclusion that hospital LOS and charges for inpatient CAP management do not differ significantly between the IV moxifloxacin and levofloxacin regimens studied. Furthermore, multivariate analyses of the total cohort showed that the choice of treatment (moxifloxacin or levofloxacin) was not a significant factor in predicting the hospital LOS or total charges.

The mean LOS of 5.51 to 5.63 days in the propensity-matched cohorts in this study is similar to mean values of 5.52 days reported in the 2005 Nationwide Inpatient Sample (NIS) and 5.27 days reported in the 2005 National Hospital Discharge Survey (NHDS) [5]. The NIS data were drawn from hospitals in 37 states that represented 78% of US community hospitals, whereas the NHDS data covered all hospitals across the 50 states. The NIS and NHDS data included all patients, whereas the present study evaluated only those ≥18 years of age.

Our findings differed somewhat from those of a similar database analysis conducted by Schein and colleagues, who retrospectively evaluated the PCD database to compare moxifloxacin and levofloxacin treatment outcomes in patients with CAP from January 2004 to December 2005 [19]. Apart from the different study time period, Schein and colleagues included patients who were hospitalized for ≥3 days but ≤90 days and who received IV moxifloxacin or IV levofloxacin through the first 3 days of hospitalization. In comparison, the present study did not limit total LOS and consequently did not exclude patients with LOS of ≥90 days, and patients were eligible for the present analysis if they started IV moxifloxacin or IV levofloxacin treatment on the day of admission or the following day and continued the regimen for ≥3 days. In addition, Schein and colleagues did not exclude patients with surgical DRGs, which may be expected to confound LOS and costs. Patients in our study tended to be older (69 years vs. 64 years) and were more likely to be female (58% vs. 52%), reside in the Northeast (15% vs. 12%), not the South (49% vs. 58%), and were admitted from the emergency department (79% vs. 71%) than those in the Schein et al. analysis.

Mean LOS and total costs in the moxifloxacin and levofloxacin cohorts also differed across the two studies, both before and after propensity matching. For example, in the propensity-matched cohorts, Schein and colleagues found the mean LOS to be 6.37 days with moxifloxacin and 5.83 days with levofloxacin ($P = 0.02$) [19], compared to 5.63 days and 5.51 days, respectively, in the present analysis ($P = 0.462$). Schein and coworkers also reported total per-patient charges of $7767 with moxifloxacin and $7638 with levofloxacin ($P > 0.05$), compared to $6624 and $6473 ($P = 0.476$), respectively, in this study. Given the considerable overlap in time periods between the two studies, differences in management practices, such as greater use of short-course therapy, cannot explain the differences between studies.

Several methodological factors may have contributed to differences between the two studies. First, Schein and colleagues performed propensity matching on approximately 60 variables, and, after matching, only the number of patients who were admitted to urban hospitals differed between treatment groups [19]. Although this appears to be a good match, the mean propensity score still differed significantly between the moxifloxacin and levofloxacin matched cohorts ($P < 0.001$) possibly because an unusually high caliper score of 0.7 was used. The standard method is to use one quarter of the standard deviation of the estimated propensity score, so it is unclear why 0.7 was chosen in their analysis. Second, Schein and colleagues excluded all patients with LOS of ≥90 days, whereas no LOS limit was placed on patient inclusion in this analysis. Although the impact of this exclusion criterion is unknown, it does represent a factor that would influence the calculation of LOS and cost. Third, the multivariate regression analyses performed after propensity

matching in the study by Schein and colleagues seemed to include only a limited number of variables (i.e., urban hospital location, treatment, and the interaction between urban location and treatment). Urban location was included as an independent variable because it remained significantly different between treatment cohorts after propensity matching. Notably, variables that are expected to affect LOS and costs and that were statistically significant in our models, such as comorbidities, severity, complications, hospital teaching status, and hospital admission via the emergency department, were omitted from the regression models used by Schein and colleagues.

Treatment consistency—defined in the present study as the absence of retreatment with the first study drug or switching to or adding another IV antibiotic—was evaluated as a secondary outcome in the present study. In the propensity-matched cohort, treatment consistency was achieved by 82.8% of patients who received moxifloxacin and 78.0% of those who received levofloxacin. Logistic regression analysis also demonstrated that treatment with moxifloxacin significantly increased the likelihood of treatment consistency when compared with levofloxacin.

Potential Study Limitations

The retrospective database design of this study has potential limitations. First, because patients were not randomly allocated to treatment, propensity score matching was needed to generate well-balanced cohorts for comparisons between moxifloxacin and levofloxacin, based on measured demographic and clinical characteristics of the patients as well as measured payor and hospital characteristics. Nevertheless, propensity score matching can be conducted only, based on observable characteristics (demographic, clinical, hospital, and payor characteristics) in the database [27]. Characteristics not captured in the database, such as physician preference, formulary restriction, causative pathogen, and antimicrobial resistance rates, could still be different between the two cohorts. In addition, as in any other retrospective administrative claims database analysis, patient-level data were somewhat limited. Although we feel that our propensity score matching protocol, including multivariate analysis post matching, effectively generated two very similar cohorts, our findings do not serve as a substitute for randomization of patients into the two treatment groups in terms of excluding certain forms of bias (e.g., selection bias, treatment-selection bias/confounding by indication). As another potential limitation, treatment consistency, as operationally defined for the first time in the present study as the absence of retreatment with the first study drug or switching to or adding another IV antibiotic, needs to be further evaluated and/or validated in distinct populations.

Conclusions

Inpatient management of CAP using IV moxifloxacin 400 mg or IV levofloxacin 750 mg daily was associated with similar hospital LOS and total costs in balanced patient populations in the present retrospective database analysis. Initial treatment with IV moxifloxacin significantly increased the likelihood of treatment consistency when compared with initial IV levofloxacin treatment using our study criteria. Both fluoroquinolones are recognized as appropriate options for empiric therapy of CAP in hospitalized patients. On the basis of the present findings, there were no significant differences between these fluoroquinolones in hospital LOS or overall costs for the management of CAP in the hospital setting.

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